# Heart Failure Pharmacotherapy

**Based on the 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure and the 2023 ACC Expert Consensus Decision Pathway on Management of HFpEF**

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**References:**
[1] Classes of Heart Failure. American Heart Association. May 31, 2017. https://www.heart.org/en/health-topics/heart-failure/what-is-heart-failure/classes-of-heart-failure
[2] Heidenreich PA, Bozkurt B, Aguilar D, et al. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines [published correction appears in Circulation. 2022 May 3;145(18):e1033]. Circulation. 2022;145(18):e895-e1032. doi:10.1161/CIR.0000000000001063
[3] Kittleson M, Panjrath G, et al. 2023 ACC Expert Consensus Decision Pathway on Management of Heart Failure With Preserved Ejection Fraction. J Am Coll Cardiol. 2023. doi:10.1016/j.jacc.2023.03.393


## Heart Failure Categories

### Stage

**A**
**At risk for HF**
- No HF signs/symptoms
- No structural/functional heart disease
- No abnormal biomarkers

**B**
**Pre-HF**
- No HF signs/symptoms
- **ONE** of the following:
  (1) Structural heart disease
  (2) ↑ filling pressures
  (3) Risk factors **PLUS** ↑ natriuretic peptides **OR** persistently ↑ cardiac troponin w/o competing diagnosis

**C**
**Symptomatic HF**
- Structural heart disease **AND**
- Current or previous HF symptoms

**D**
**Advanced HF**
- HF symptoms interfering with normal activity and/or recurrent HF hospitalizations (despite GDMT)

### LVEF

**HFrEF** *(reduced EF)* — **LVEF ≤ 40%**

**HFimpEF** *(improved EF)* — **LVEF > 40%** *(upon follow up after a previous measurement of LVEF ≤ 40% )*

**HFmrEF** *(mildly reduced EF)* — **LVEF 41-49%** *(w/ evidence of spontaneous/provokable ↑ LV filling pressures)*

**HFpEF** *(preserved EF)* — **LVEF ≥ 50%** *(w/ evidence of spontaneous/provokable ↑ LV filling pressures)*

### NYHA Class

**I**
- No symptoms from ordinary daily activities

**II**
- No symptom at rest
- Ordinary daily physical activities cause HF symptoms

**III**
- No symptom at rest
- Activities lighter than ordinary daily physical activities cause HF symptoms

**IV**
- Symptoms at rest
- Discomfort worsens with physical activities

## Goals of Therapy

**Stage A**
- Primary prevention of heart failure

**Stage B**
- Prevention of clinical heart failure

**Stage C**
- Reduction of mortality
- Reduction of heart failure symptoms and hospitalization risk
- Elimination of potential barriers to self-care

**Stage D**
- Provision of inotropic support until mechanical circulatory support or cardiac transplantation is available
- Palliative symptom control and functional improvement (if not eligible for mechanical circulatory support or cardiac transplantation)

## Pharmacotherapy Recommendations

### Stage A
- Control BP in patients with hypertension
- SGLT2i in patients with T2DM **plus:**
  - Established CVD **or,**
  - High CV risk
- Manage existing comorbidities

### Stage B
- ACEi and evidence-based BB in patients with LVEF ≤ 40%
  - If LVEF ≤ 40% **and recent MI**, use ARB if ACEi is not tolerated

### Stage C (HFpEF)
- SGLT2i in **all patients** with HFpEF *(unless contraindicated)*
- May consider MRA and/or ARNi if LVEF < 55-60%
  - May consider regardless of LVEF for female patients
  - May consider ARB if unable to receive ARNi therapy
- PRN loop diuretic

### Stage C (HFmrEF)
- PRN diuretics (**loop** preferred)
- SGLT2i may be beneficial
- May consider MRA, ACEi/ARB/ARNi, and evidence-based BB *particularly* if LVEF is closer to **HFrEF threshold**

### Stage C (HFimpEF)
- Continue GDMT
  - Even if asymptomatic

### Stage C (HFrEF)

#### All patients
- **ARNi** or **ACEi** or **ARB**
  - ARNi: NYHA class II-III
  - ACEi or ARB: NYHA class II-IV
  - Order of preference: ARNi > ACEi > ARB
  - **36-hour washout** required when switching between ACEi and ARNi (and vice versa)
- **Beta Blocker** (evidence-based)
  - Bisoprolol, carvedilol, metoprolol succinate
- **MRA** (e.g. eplerenone, spironolactone)
  - NYHA class II-IV
  - eGFR > 30 mL/min/1.73m2
  - Serum potassium < 5 mEq/L
- **SGLT2i**
  - With or without T2DM
- **Diuretics** (as needed)
  - Loop diuretics preferred

#### Specific patients
- **Hydralazine + isosorbide dinitrate**
  - African American patients on optimal therapy
  - NYHA class III-IV
- **Ivabradine**
  - NYHA class II-III and LVEF **≤ 35%**
  - On GDMT including **max tolerated BB**
  - NSR with resting HR ≥ 70 BPM
- **Vericiguat**
  - NYHA class II-IV and LVEF **< 45%**
  - Recent HF worsening
  - ↑ BNP or NT-proBNP
- **Digoxin**
  - If symptomatic despite GDMT **or**
  - Unable to tolerate GDMT
- **Potassium binders**
  - e.g., **Patiromer**, **sodium zirconium cyclosilicate**
  - Patients with hyperkalemia (K+ ≥ 5.5 mEq/L) while on RAASi
- **Omega-3 PUFA** (may consider as an adjunct)
  - NYHA class II-IV

### Selected Medications That May Cause or Exacerbate HF

| | |
|---|---|
| **COX inhibitors (e.g., NSAIDs)** | • ↑ H2O retention, ↑ vascular resistance, ↓ response to diuretics<br>• **Immediate** onset, **major** induction/precipitation of HF |
| **Thiazolidinediones** | • Potential blockage of calcium channel<br>• **Intermediate** onset, **major** induction/precipitation of HF |
| **Saxagliptin, Alogliptin** | • Mechanism is unclear<br>• **Immediate or delayed** onset, **major** induction/precipitation of HF |
| **Flecainide, Disopyramide** | • Proarrhythmic, negative inotropic effects<br>• **Immediate to intermediate** onset, **major** induction/precipitation of HF |
| **Sotalol** | • Proarrhythmic effects, beta blockade<br>• **Immediate to intermediate** onset, **major** induction/precipitation of HF |
| **Dronedarone** | • Negative inotropic effects<br>• **Immediate to intermediate** onset, **major** induction/precipitation of HF |
| **Doxazosin** | • Beta-1 stimulation, ↑ renin and aldosterone<br>• **Intermediate to delayed** onset, **moderate** induction/precipitation of HF |
| **Diltiazem, Verapamil** | • Negative inotropic effects<br>• **Immediate to intermediate** onset, **major** induction/precipitation of HF |
| **Nifedipine** | • Negative inotropic effects<br>• **Immediate to intermediate** onset, **moderate** induction/precipitation of HF |

Recreated from Table 13 from the 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure

### Abbreviations

**ACEi:** angiotensin-converting enzyme inhibitors
**ARB:** angiotensin (II) receptor blocker
**ARNi:** angiotensin receptor-neprilysin inhibitors
**BB:** beta-blocker
**BNP:** B-type natriuretic peptide
**BP:** blood pressure
**CVD:** cardiovascular disease
**eGFR:** estimated glomerular filtration rate
**GDMT:** guideline-directed medical therapy
**HF:** heart failure
**HFimpEF:** heart failure with improved ejection fraction
**HFmrEF:** heart failure with mildly reduced ejection fraction
**HFpEF:** heart failure with preserved ejection fraction
**HFrEF:** heart failure with reduced ejection fraction
**LV:** left ventricular
**LVEF:** left ventricular ejection fraction
**MI:** myocardial infarction
**MRA:** mineralocorticoid receptor antagonist
**NT-proBNP:** N-terminal prohormone of B-type natriuretic peptide
**NYHA:** New York Heart Association
**PRN:** as needed
**PUFA:** polyunsaturated fatty acid
**RAASi:** renin-angiotensin-aldosterone system inhibitor
**SGLT2i:** sodium-glucose cotransporter-2 inhibitor
**T2DM:** type 2 diabetes mellitus


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